CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 75-318

CORRESPONDENCE

invamed inc.
732-274-2400 Fax: 732-274-8989
2400 Rt. 130 North, Dayton, New Jersey 08810

NEW DOMESTIC
NC

February 5, 1999

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

FACSIMILE AMENDMENT

Re: **TICLOPIDINE HYDROCHLORIDE TABLETS, 250 mg**
ANDA # 75-318
FACSIMILE AMENDMENT

Dear Sirs:

I have herewith enclosed a "*FACSIMILE AMENDMENT*" document (submitted in duplicate) to our pending application for **TICLOPIDINE HYDROCHLORIDE TABLETS, 250 mg (ANDA # 75-318)** as required under 21 CFR 314.120.

The firm has submitted an additional copy of this facsimile amendment to the U.S. Food and Drug Administration, New Jersey District Office. We hereby certify that this additional copy (field copy) is a true copy of the Archival and Review copies of the facsimile amendment.

Sincerely,

Mahendra Patel, Ph.D.
Vice President

RECEIVED
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GENERIC DRUGS

ANDA 75-318

Invamed Inc.
Attention: Mahendra Patel, Ph.D.
2400 Route 130 North
Dayton, NJ 08810

Dear Madam:

This is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Ticlopidine Hydrochloride Tablets, 250 mg (Ticlopidine).

In light of several new applicants seeking to market Ticlopidine, inquiries from those applicants, and the November 27, 1998, citizen petition from Hoffmann-LaRoche, Inc., as well as other correspondence, the Agency has reevaluated the measures that it believes may enhance the safe use of Ticlopidine.

Our letter of September 21, 1998, informed you that Hoffman-LaRoche, Inc., manufacturer of the reference listed drug, TICLID® tablets, has in place a number of steps intended to encourage the safe use of their product. These steps include offering free blood monitoring to patients and providing educational materials to health-care professionals to make them aware of potentially life-threatening hematological adverse reactions associated with the drug and to help ensure appropriate monitoring of patients on Ticlopidine.

The Agency has reevaluated the utility of Hoffman-LaRoche's post-marketing program in light of information gathered from their seven years of experience marketing TICLID®. We have concluded that the provision of white cell count monitoring, offered free of charge, does not significantly enhance the safe use of the product. Accordingly, although monitoring remains an important part of the safe use of Ticlopidine, we will not expect applicants to offer this free service in the future. We continue to believe strongly, however, that a post-approval educational program directed towards prescribing physicians and other health-care professionals may enhance the safe use of Ticlopidine.

The Agency believes that an effective educational program for Ticlopidine should include the following characteristics:

1. Target audience for an adequate educational campaign.

   a. Physicians, including those within a health-care system such as an HMO or PPO, who prescribe Ticlopidine.

   b. Other health-care professionals, such as nurse practitioners, physician assistants, and dispensing pharmacists, who are in a position in a given health-care system to educate patients and/or monitor compliance.

2. Substantive elements of an adequate educational campaign.

   a. A clear statement that Ticlopidine is approved for use only in patients who are intolerant or allergic to aspirin therapy or who have failed aspirin therapy.

   b. Discussion of the known risks of Ticlopidine therapy and how to mitigate them. An adequate discussion would include not only information about the frequency and potential severity of adverse events, but also informaiton about the role that clinical observation and blood monitoring can play in preventing/minimizing their clinical severity. The discussion should include information about the following known adverse events:

      (i) Neutropenia/agranulocytosis;

      (ii) Thrombotic thrombocytopenic purpura (TTP); and

      (iii) Aplastic anemia.

   c. Information delineating the schedule for blood and clinical monitoring during the first three months of treatment, and describing the steps to be taken should the results of such monitoring be abnormal.

   d. A statement reinforcing the need for all health-care professionals to report observed serious and fatal adverse events with Ticlopidine administration to MedWatch.

Within 10 days of receiving this notice, we ask that you submit your post-approval plan to address the important issues outlined above. You should be prepared to implement your educational program upon distribution and marketing of Ticlopidine under an approved application. You should also provide, in each annual report, a brief summary of your implementation efforts, as well as any other relevant data, associated with the educational program described above.

We await your prompt response. If you have further questions or need clarification on any of the elements listed above, please contact Mr. Charlie Hoppes, Team Leader - Division II; Labeling Review Branch at (301) 827-5846.

Sincerely yours,

/S/ 6/15/99

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

invamed inc.
732-274-2400 Fax: 732-274-8989
2400 Rt. 130 North, Dayton, New Jersey 08810

July 2, 1998

ORIG AMENDMENT
N/A

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

MAJOR AMENDMENT

Re: **TICLOPIDINE HYDROCHLORIDE TABLETS, 250 mg**
ANDA # 75-318
MAJOR AMENDMENT

Dear Sirs:

I have herewith enclosed a "*MAJOR AMENDMENT*" document (submitted in duplicate) to our pending application for **TICLOPIDINE HYDROCHLORIDE TABLETS, 250 mg (ANDA # 75-318)** as required under 21 CFR 314.120.

The firm has submitted an additional copy of this major amendment to the U.S. Food and Drug Administration, New Jersey District Office. We hereby certify that this additional copy (field copy) is a true copy of the Archival and Review copies of the major amendment.

Sincerely,

M. Patel

Mahendra Patel, Ph.D.
Vice President

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GENERIC DRUGS

- You must submit a copy of a final order or judgement from which no appeal may be taken (which might not be the one from the District Court), or a settlement agreement between the parties, whichever is applicable, or a licensing agreement between you and the patent holder, or any other relevant information. We ask that this information be submitted promptly to the application.

If you have further questions you may contact Peter Rickman, Chief, Regulatory Support Branch, at (301)827-5862.

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Kassandra Sherrod
Project Manager
(301) 827-5849

Sincerely yours,

/S/

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 75-318

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Endorsement: HFD-615/PRickman, Chief, RSB 4/6/98 date
HFD-615/GDavis, CSO 2/10/98 date
HFD-645/BArnwine, Sup. Chem. _____ date
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FT/njg/2/10/98
ANDA Acknowledgment Letter!

invamed inc.
732-274-2400 Fax: 732-274-8989
2400 Rt. 130 North, Dayton, New Jersey 08810

June 28, 1999

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

MINOR AMENDMENT

Re: **TICLOPIDINE HYDROCHLORIDE TABLETS, 250 mg**
ANDA # 75-318

To Fax

Dear Sirs:

I refer to your letter dated June 15, 1999. The firm agrees with the Agency's belief that an effective educational program for **TICLOPIDINE HYDROCHLORIDE** is essential. The firm is proposing to implement this educational program as follows:

1. Educational campaign will focus the following audience:

   (a) Physician's (including those within a health-care system such as an HMO or PPO)
   (b) Other Health-care professionals, such as nurse practitioners, physician assistants, and pharmacists, who are in a position to educate patients and/or monitor compliance.

   In order to effectively achieve this goal, the firm will provide, "Dear Doctor Letter", "Dear Pharmacist Letter", Product Monograph, Patient Educational Booklet and other relevant literature.

2. The proposed educational campaign will include following elements:

serious and fatal adverse events with Ticlopidine administration to MedWatch.

The firm will implement the proposed educational program upon distribution and marketing of TICLOPIDINE HYDROCHLORIDE TABLETS, 250 mg. The complete information and relevant documents will be submitted as part of ANDA. The same information will also be submitted to DDMAC as part of post-approval educational plan.

Sincerely,

M. R. Patel

Mahendra Patel, Ph.D.
Vice President